

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Applicant: Jacobus M. Lemmens et al.

Title: *Paroxetine Compositions and Processes for Making the Same*

Appl. No.: 10/678,082

Filing Date: 10/6/2003

Examiner: Chris E. SIMMONS

Art Unit: 1612

Confirmation 4414

Number:

**BRIEF ON APPEAL**

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Sir:

Under the provisions of 37 C.F.R. § 41.37, this Appeal Brief is being filed together with a credit card payment form in the amount of \$540.00 covering the 37 C.F.R. 41.20(b)(2) appeal fee. If this fee is deemed to be insufficient, authorization is hereby given to charge any deficiency (or credit any balance) to the undersigned deposit account 19-0741.

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**I. REAL PARTY IN INTEREST**

The real party in interest is NOVEN THERAPEUTICS, LLC, which acquired rights to the present application through an assignment recorded on March 2, 2010, on Reel/Frame 024006/0417.

**II. RELATED APPEALS AND INTERFERENCES**

None.

**III. STATUS OF CLAIMS**

Pending claims: 51-59.

Rejected claims: 51-59.

Objected to claims: none.

Withdrawn claims: none.

Appealed claims: 51-59.

**IV. STATUS OF AMENDMENTS**

Appellants last amended the claims in a response filed on February 11, 2009. The claims have not been further amended since that time.

**V. SUMMARY OF CLAIMED SUBJECT MATTER**

Appealed, independent claim 51 is directed to a pharmaceutical composition that comprises a sulfonate salt of paroxetine.<sup>1</sup> The composition further comprises calcium hydrogen phosphate anhydride in the form of plate shaped crystals of agglomerates thereof<sup>2</sup> and it comprises a disintegrant and lubricant.<sup>3</sup> However, the composition does not contain lactose or microcrystalline cellulose.<sup>4</sup> Finally, the claimed composition has a pH within the range of 5.0 to 6.0.<sup>5</sup>

Appealed, independent claim 51 is directed to a pharmaceutical composition that comprises a sulfonate salt of paroxetine,<sup>6</sup> calcium hydrogen phosphate anhydride in the form of plate shaped crystals of agglomerates thereof,<sup>7</sup> a disintegrant and lubricant,<sup>8</sup> and that has a pH within the range of 5.0 to 6.0.<sup>9</sup> The composition has an added water content of 1.2 wt% or less.<sup>10</sup>

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<sup>1</sup> See specification at page 3, line 30 to page 4, line 1. See also specification at page 5, lines 6 and 21-22.

<sup>2</sup> See specification (as amended on Oct. 17, 2007) at page 13, lines 6-7.

<sup>3</sup> See specification, page 4, line 3 and page 6, lines 18-19.

<sup>4</sup> See specification, page 8, lines 12-14.

<sup>5</sup> See specification, page 7, line 22.

<sup>6</sup> See specification at page 3, line 30 to page 4, line 1. See also specification at page 5, lines 6 and 21-22.

<sup>7</sup> See specification (as amended on Oct. 17, 2007) at page 13, lines 6-7.

<sup>8</sup> See specification, page 4, line 3 and page 6, lines 18-19.

<sup>9</sup> See specification, page 7, line 22.

<sup>10</sup> See specification, page 8, lines 31-31.

**VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

The only rejection is against claims 51-59 for being allegedly unpatentable under 35 U.S.C. § 103(a) over U.S. Patent No. 6,113,944 to Pathak *et al.* ("Pathak") in view of U.S. Patents No. 5,874,447 to Benneker *et al.* ("Benneker") and No. 4,675,188 to Chu.

## VII. ARGUMENT

The Examiner's sole rejection of claims 51-59 embodies clear legal and factual error.

Accordingly, Appellants respectfully urge the Board to reverse the rejection.

The Examiner cited Pathak for alleged disclosure of paroxetine formulations with excipients such as calcium phosphate, sodium starch glycolate and magnesium stearate.<sup>11</sup> The Examiner acknowledge that Pathak does not, however, teach or suggest the use of a sulfonate salt of paroxetine or calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates.<sup>12</sup> Moreover, the Examiner acknowledge that Pathak does not teach or suggest that the paroxetine formulations have a pH of 5.0 to 6.0.<sup>13</sup>

Benneker was cited for alleged teaching of sulfonate salts of paroxetine.<sup>14</sup> Further, the Examiner cited Benneker for alleged suggestion that such salts exhibit greater solubility.<sup>15</sup>

Finally, the Examiner cited Chu for teaching the use of calcium hydrogen phosphate anhydrate ("CHP") for direct compression tabletting.<sup>16</sup> Critical to the stated rejection, the Examiner relied upon Chu also for its teachings regarding pH, as discussed in more detail below.<sup>17</sup>

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<sup>11</sup> See Non-final Office Action dated January 1, 2008, page 2.

<sup>12</sup> *J.d.*

<sup>13</sup> See Non-final Office Action dated January 1, 2008, page 3.

<sup>14</sup> *J.d.*

<sup>15</sup> *J.d.*

<sup>16</sup> *J.d.*

<sup>17</sup> See Non-final Office Action dated January 1, 2008, page 4.

The rejection hinges upon at least two errors. First, the Examiner contended that the "prior art suggest[s] a composition that is substantially identical to that which is claimed . . ." and, hence, the prior art compositions would "reasonably be considered" to possess the claimed pH of 5.0 to 6.0.<sup>18</sup>

Second, the Examiner asserted that because Chu teaches a pH of a reaction medium in which calcium hydrogen phosphate ("CHP") can be prepared, then the final product, CHP, "is reasonably considered to maintain a similar – if not the same – pH when mixed with the active ingredients to form the tablet,"<sup>19</sup> even though no scientific theory supports this extrapolation of pH of a component, CHP, to pH of a composition containing that component. The Examiner asserted in this regard that Chu teaches pH adjustment of the reactions that produce CHP; hence, according to the Examiner, pH can affect "the shape and size of [CHP] particles," by identifying pH as a parameter suitable for optimizing.<sup>20</sup> Based upon this assertion, the Examiner concluded that "the pH [of the claimed composition] is still reasonably considered to be the same."<sup>21</sup>

#### A. Chu Does Not Suggest pH of a Composition that Contains Calcium Hydrogen Phosphate

The rejection is founded on factual error because the only pH discussed by Chu is that of a reaction medium from which anhydrous dicalcium phosphate is ultimately isolated.<sup>22</sup> Chu does

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<sup>18</sup> Final Office Action dated May 11, 2010 at page 3; *see also* Interview Summary dated October 13, 2009.

<sup>19</sup> Final Office Action dated May 11, 2010, page 4 (emphasis added)

<sup>20</sup> Final Office Action dated May 11, 2010, page 3

<sup>21</sup> Final Office Action dated May 11, 2010, page 4

<sup>22</sup> *See* Chu at col. 1, line 64 to col. 2, line 8 and at col. 3, lines 42-48.

not teach the pH of any resulting CHP product nor does the reference hint at pH of a pharmaceutical composition that comprises the CHP product. Chu's disclosure of pH is irrelevant to the claimed invention not because such pH applies in a different context, but because it describes a completely different substance, a reaction medium, not a pharmaceutical composition comprising CHP and other components, as claimed.

Because Chu utterly fails to teach or suggest pH of its anhydrous dicalcium phosphate, the skilled artisan has no reasonable expectation that Chu's CHP product will possess a given pH. Even if it is assumed, *arguendo*, that Chu does somehow suggest a pH of its CHP product, there still remains no reasonable expectation that a composition comprising Chu's CHP product together with an active agent and other excipients would have a pH of 5.0 to 6.0, as prescribed by the rejected claims.

Apparently responsive to these considerations, the Examiner highlighted teaching in Appellant's own specification that pH of a composition can be adjusted by selection of excipients, such as dicalcium phosphate, which can be acidic or neutral, depending on the particular species of dicalcium phosphate and how it is processed during manufacture.<sup>23</sup> Yet, this is a legal red herring that cannot support an obviousness rejection, which must be based on the teachings of the prior art.

What is relevant here is that none of the cited prior art references, such as Chu, gives the skilled artisan a reason to adjust pH of dicalcium phosphate, teaches how to adjust pH, or

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<sup>23</sup> Final Office Action dated May 11, 2010, page 4

indicates what pH might pertain to a composition that contains dicalcium phosphate of a given pH. Simply put, no combination of the cited prior art teaches or suggests a composition having pH within the range 5.0 to 6.0, as claimed. Accordingly, there is not even a *prima facie* cases of obviousness.

The rejection devolves essentially to the fact-starved allegations that (i) Chu teaches pH of dicalcium phosphate (which it does not), and (ii) pH is an attribute of a pharmaceutical composition comprising the dicalcium phosphate. Because both allegations get nowhere near the claimed invention without factual and legal errors to bridge the gap, the rejection is improper and should be withdrawn.

**B. The Cited Prior Art Does Not Suggest a Composition that Inherently Possesses a pH of 5.0 to 6.0**

The rejection also manifests legal error by veiling a doctrine of inherency<sup>24</sup> in a conclusion that prior art “ingredients,” when combined, would “reasonably be considered to have similar pH values [as the claimed composition] unless otherwise proven.”<sup>25</sup> The Examiner’s reasoning, in essence, arrives at precisely the same point from which it departs: since a known composition possesses certain properties, *ipso facto*, then no such property can be unexpected for purposes of a section 103 analysis.

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<sup>24</sup> The Final Office Action does not actually invoke the term “inherency”, *per se*, but it does cite to MPEP § 2112.01 [R-3], which explicitly elaborates upon the doctrine of inherency in anticipation and obviousness rejections. Final Office Action dated May 11, 2010, page 4.

<sup>25</sup> Final Office Action dated May 11, 2010, page 3

Yet, by the Examiner's own admission, the claimed composition is not known, *per se*, but rather at best would have been obvious from the combined teachings of Pathak, Benneker, and Chu. The factual and legal errors surrounding this assertion are outlined above. Given the fact that none of the cited references hint at pH of any "ingredient," much less of the composition as a whole (as claimed), there is no factual basis for the assertion that a hypothetical composition that might be made by selecting and combining different components from the cited references, and that would possess a pH within the range of 5.0 to 6.0 as claimed. The pH of CHP is not fixed, but instead varies according to its method of manufacture. Hence, a composition that comprises CHP does not necessarily possess the presently recited pH of 5.0 to 6.0. The Examiner therefore erred by relying upon inherency in this context.

Indeed, the specification sets forth countervailing evidence that rebuts a rejection based on inherency by showing that any putative prior art composition does not "necessarily possess the characteristics of the claimed product."<sup>26</sup> The application presents in some detail that commercially available CHP is "generally alkaline; i.e. pH greater than 7 . . ."<sup>27</sup> For instance, the product DI-TAB has a pH of about 7.4.<sup>28</sup> Yet, some CHP gives rise to acidic or neutral pH, which depends on the form and grade of CHP and whether and to what extent impurities remain in the CHP after processing.<sup>29</sup> Still, CHP is generally acknowledged to have a pH of about 7.3.<sup>30</sup>

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<sup>26</sup> *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977).

<sup>27</sup> Specification, page 7 (emphasis added)

<sup>28</sup> *Id.*

<sup>29</sup> Specification, pages 7-8

<sup>30</sup> Specification, page 8

The pH of a composition can be governed by a blend of CHP products, each having their different respective pH values, and by excipients other than CHP.<sup>31</sup> Accordingly, the skilled artisan cannot know *a priori* the pH of a given CHP-containing composition. Because Chu does not teach the pH of its anhydrous dicalcium phosphate, there is no basis for the assertion that pH of Chu's CHP and, allegedly, the pH of a composition comprising that CHP, falls within the claimed range of 5.0 to 6.0. To the extent that the skilled artisan might attribute a particular pH to the CHP taught by Chu, it likely would be a basic pH (e.g., greater than 7), as taught in the application for most CHP. Thus, there is absolutely no basis for the Examiner's conclusion that Chu could be understood to directly or inherently suggest the pH of the claimed compositions.

For all of these reasons, the cited combination of Pathak, Benneker, and Chu fails to render obvious the claimed composition. Accordingly, Appellants respectfully urge withdrawal of the rejection.

Respectfully submitted,

By   
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Date December 6, 2010

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<sup>31</sup> *Id.*

**VIII. CLAIMS APPENDIX**

51. (Previously presented). A pharmaceutical composition comprising a sulfonate salt of paroxetine, calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, a disintegrant and a lubricant, wherein said composition does not contain lactose or microcrystalline cellulose, and wherein said composition has a pH within the range of 5.0 to 6.0.

56. (Previously Presented). A pharmaceutical composition comprising a sulfonate salt of paroxetine, calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, a disintegrant and a lubricant, wherein said composition has a pH within the range of 5.0 to 6.0 and said composition has an added water content of 1.2 wt% or less.

**IX. EVIDENCE APPENDIX**

1. A-TAB Trademark records and product data sheet entered into the record on October 17, 2007.
2. U.S. Patent No. 3,095,269 entered into the record on July 8, 2008.



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### Typed Drawing

Word Mark	A-TAB
Goods and Services	IC 001, US 001 005 006 010 026 046. G & S: anhydrous dicalcium phosphate for use in tabletting. FIRST USE: 19851007. FIRST USE IN COMMERCE: 19851007
Mark Drawing Code	(1) TYPED DRAWING
Serial Number	74687971
Filing Date	June 7, 1995
Current Filing Basis	1A
Original Filing Basis	1A
Published for Opposition	January 16, 1996
Registration Number	1967070
Registration Date	April 9, 1996
Owner	(REGISTRANT) Rhone-Poulenc Inc. CORPORATION NEW YORK Black Horse Lane Monmouth Junction NEW JERSEY 085435266
(LAST LISTED OWNER) INNOPHOS, INC. CORPORATION DELAWARE 259 PROSPECT PLAINS ROAD CRANBURY NEW JERSEY 08512	
Assignment Recorded	ASSIGNMENT RECORDED
Type of Mark	TRADEMARK
Register	PRINCIPAL
Affidavit Text	SECT 8 (6-YR). SECTION 8(10-YR) 20051227.
Renewal	1ST RENEWAL 20051227
Live/Dead Indicator	LIVE

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**Typed Drawing**

Word Mark	A-TAB
Goods and Services	(CANCELLED) IC 001, US 006, G & S. ANHYDROUS DICALCIUM PHOSPHATE FOR USE IN TABLETING. FIRST USE: 19851007. FIRST USE IN COMMERCE: 19851007
Mark Drawing Code	(1) TYPED DRAWING
Serial Number	73565174
Filing Date	October 25, 1985
Current Filing Basis	1A
Original Filing Basis	1A
Published for Opposition	March 4, 1986
Registration Number	1394542
Registration Date	May 27, 1986
Owner	(REGISTRANT) STAUFFER CHEMICAL COMPANY CORPORATION DELAWARE WESTPORT CONNECTICUT 068810850
Assignment Recorded	ASSIGNMENT RECORDED
Attorney of Record	PAUL J. JUETTNER
Prior Registrations	1136524;1258467;1318808
Type of Mark	TRADEMARK
Register	PRINCIPAL
Live/Dead Indicator	DEAD
Cancellation Date	November 30, 1992

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## A-TAB (1/2)

## PRODUCT DATA SHEET ORG FP ATAB APR2007

<u>IDENTIFICATION</u>	CAS n° [7789-77-7]
<u>SYNONYM</u>	Dibasic Calcium Phosphate Anhydrous Phosphoric acid, calcium salt (1:1) Calcium Phosphate, Anhydrous (1:1) Calcium Hydrogen Phosphate Anhydrous Calcii hydrogenophosphas anhydricus
<u>EMPIRICAL FORMULA</u>	CaHPO <sub>4</sub>
<u>MOLECULAR WEIGHT</u>	M <sub>r</sub> = 136.1
<u>PHYSICO-CHEMICAL PROPERTIES</u>	White, odourless and tasteless granules. Practically insoluble in cold water and in ethanol (96 per cent). It dissolves in dilute hydrochloric acid and in dilute nitric acid.
<u>APPLICATIONS</u>	Used as excipient in the manufacture of medicinal and nutraceutical products an as a source of calcium and phosphorus in nutritional supplements.
<u>SPECIFICATIONS</u>	The specifications below are the harmonized specifications in force in the EU since April 1, 2007 and the US as of December 1, 2007 (USP 30, S2) – Considering some specifications are not harmonized, our sales specifications are based on the most restrictive ones
Specification items	Limits Comment (non harmonized attributes)
Assay (as CaHPO <sub>4</sub> ·2 H <sub>2</sub> O)	98.0 – 103.0 %
Loss on Ignition	6.6 – 8.5 %
Chlorides	0.25 % max
Fluorides	50 ppm max.
Sulphates	0.5 % max
Arsenic	3 ppm max.
Lead (FCC)	2 ppm max.
Heavy metals (as Pb)	0.003 % max.
Carbonate Passes test	
Barium Passes test	
Acid insoluble substances	0.2 % max
Iron	400 ppm max.
Particle Size (wet sieving)	
On 20 # (850 µm)	1 % max
On 100 # (150 µm)	40 % min
Through 200 # (75 µm)	25 % max
Through 325 # (45 µm)	5 % max

Innophos, Inc.  
P.O. Box 8000  
Cranbury, NJ 08512-8000, USA



All information is offered in good faith, without guarantee or obligation for the accuracy or sufficiency thereof, or the results obtained, and is accepted at user's risk. Nothing herein shall be construed as a recommendation for uses which infringe valid patents or as extending license under valid patents.



## A-TAB (2/2)

TYPICAL PROPERTIES

pH (20 % slurry)	5
Bulk Density	0.80 g/ml (50 lbs/ft <sup>3</sup> )
Calcium content	29.1 %
Phosphorus content	22.6 %
Lead	0.25 ppm
Particle size (wet sieving)	
On     20 # ( 850 µm)	0 %
Through 100 # ( 150 µm)	35 %
Through 200 # ( 75 µm)	10 %
Through 325 # ( 45 µm)	3 %

REGULATORY / QUALITY

Regulatory support is provided to assist our customers in their registration process.

The following declarations can be downloaded on  
<http://www.innophos.com/certs.asp>

Allergen:	Free of Allergens
GMO	Free of Genetically Modified Organisms
Halal	Product Conforms to Halal Standards
ISO	ISO-9001: 2000 (NSH-ISR)
Kosher	Product Conforms to Kosher Standards
NAFTA	Product Qualifies for the North-American Free Trade Agreement
NSF1 and NSF2 International – Product conforms to NSF Standard 60	
BSE/TSE	No materials of animal origin are used

Residual Solvents The product is free of Residual Solvents

PACKAGING

25 kg net weight paper bags

TRANSPORT

- |   |                                     |               |
|---|-------------------------------------|---------------|
| <input type="checkbox"/> INLAND             | International Legislation (RID-ADR) | Not regulated |
| <input type="checkbox"/> SEA FREIGHT (OMI)  |                                     |               |
| <input type="checkbox"/> AIR FREIGHT (IATA) |                                     |               |

STORAGE CONDITIONS

Keep the product in the original unopened container away from moisture and heat, in normal pharmaceutical warehousing conditions.

Re-test date: 3 years

SAFETY INSTRUCTIONS

Please consult the material safety data sheet, downloadable on <http://www.innophos.com>

WARNING TO USERS

The information contained in this document is given in good faith, based on our current knowledge. It is only an indication and is in no way binding, particularly as regards infringement or pre-emption to third party rights through the use of our products. We give no guarantee of the results obtained by the user. This information must on no account be used as a substitute for necessary prior tests which alone can ensure that a product is suitable for a given use. Users are responsible for ensuring that they have the necessary knowledge, experience and qualifications and authorizations. Users are requested to check that they are in possession of the latest version of this document and we are at their disposal to supply any additional information.



**Innophos Research and Development Center**

Innophos produces A-Tab®, an anhydrous dicalcium phosphate as an excipient for pharmaceutical products. A-Tab® is a crystalline material which grows into rhombic plate shaped crystals. Individual crystals vary in size, but most are between 15-30 um in length when measuring the longest axis. These plates form agglomerates of larger clusters with the major fraction of particles between 74 and 150 um (200 and 100 mesh). The overall particle size specification is 1% maximum on 20 Mesh, 40% minimum through 100 Mesh, 25% maximum through 200 Mesh, and 5% maximum through 325 Mesh. The agglomerated crystals are not considered very porous, having a typical surface area of 8-15 m<sup>2</sup>/g. Some other typical properties and specifications of A-Tab® can be found at [www.Innophos.com](http://www.Innophos.com) which is the source of the charts seen below.

**Typical Properties**

pH	5
Bulk Density	50
Phosphorus	22.6%
Calcium	29.1%
Lead	< 0.25 ppm
Compressibility, kp range	25 - 38
Insoluble	in Alcohol
Specifications	
Assay	98.0% min. - 105% max.
Loss on Ignition	7.0 min. - 8.5% max.
Arsenic	3 ppm max.
Fluoride	0.005% max.
Heavy Metal	(as Pb) 0.003% max.
Lead	2 ppm max.
Chloride	0.25% max.
Carbonate	Passes Test
Sulfate	0.5% max.
Barium	Passes Test
Acid Insolubles	0.2% max.

Regards,

Robert C. Finn, PhD

Sr. Staff Scientist, Innophos, Inc.

# United States Patent Office

3,095,269

Patented June 25, 1963

1

## 3,095,269 CONVERSION OF CALCIUM HYDROGEN PHOSPHATE DIHYDRATE TO THE ANHYDROUS FORM

Vincent Chiola and Clarence D. Vanderpool, Towanda, Pa., assignors to Sylvania Electric Products Inc., a corporation of Delaware  
No. Drawing. Filed Oct. 12, 1960, Ser. No. 62,097  
2 Claims. (Cl. 23—109)

This invention relates to a novel method for preparing very highly crystalline, closely-sized, luminescent grade, anhydrous dibasic calcium phosphate,  $\text{CaHPO}_4$ , possessing characteristic form and habit.

Since crystallinity and size of luminescent grade  $\text{CaHPO}_4$  are reflected in the crystallinity and size of the phosphor manufactured therefrom and ultimately in the performance of the end-product fluorescent lamp, it has been found extremely desirable to control the starting phosphate raw material used in the synthesis of calcium halophosphate phosphors.

The purpose and object of this invention is to provide anhydrous dibasic calcium phosphate for use in phosphors and possessing a high degree of crystallinity, a narrow particle size distribution, uniform crystal size, relatively little agglomeration or aggregation, optimum bulk density and characteristic, plate-like crystals.

Previous practice, used in preparing luminescent grade  $\text{CaHPO}_4$ , was to mix solutions of a calcium salt, generally calcium chloride, with diammonium phosphate (DAP) at temperatures greater than  $60^\circ\text{C}$ . The anhydrous  $\text{CaHPO}_4$  thus precipitated was washed, recovered by filtration and dried in the usual manner. An alternative practice was to mix DAP and calcium chloride solution at temperatures ranging from room temperature to  $65^\circ\text{C}$ , to precipitate calcium hydrogen phosphate dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ). After separation from its mother liquor the dihydrate was converted (dehydrated) to anhydrous material by normal drying methods.

Products prepared by the prior method of mixing hot solutions of DAP and  $\text{CaCl}_2$  are generally characterized by poor crystallinity, i.e., many fines, poorly formed crystals (spherulitic growths, etc.), wide particle size distribution, relatively high degree of agglomeration and aggregation, varying bulk density and a three dimensional type of crystal of considerable thickness. This is not the type of calcium hydrogen phosphate which is most desirable for synthesis of calcium halophosphate phosphors, useful in fluorescent lamp manufacture.

The alternative practice of drying the highly crystalline dihydrate to anhydrous  $\text{CaHPO}_4$  produces a material having many of the same disadvantages. Dehydration of the dihydrate using normal mechanical drying practices usually results in highly agglomerated and aggregated anhydrous  $\text{CaHPO}_4$ . There is, in addition, a problem of controlling drying rate to effect gradual release of large quantities of chemically bonded water or water of crystallization. Excessive rate of drying tends to cause degradation of well-formed crystals due to sudden release of the water, resulting in excessive break-up or fracture of dihydrate particles, fines and wide size distribution. Finally, this method has an economic disadvantage because of the necessity for isolating or separating the dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) before conversion (dehydration) to anhydrous  $\text{CaHPO}_4$ .

Control of the calcium hydroxyl apatite (or tricalcium phosphate) content tends to drift away from the optimum as indicated by the nominal mole ratio,  $\text{Ca}/\text{P}=1.03$ , in both the usual and alternative practice. It is extremely desirable to have a raw material of  $\text{Ca}/\text{P}$  mole ratio as close as possible to the theoretical mole ratio of 1.00 for  $\text{CaHPO}_4$ . The presence of higher phosphates makes the

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synthesis of calcium halophosphate phosphors much more critical, as is well known in the art.

We have found that calcium hydrogen phosphate dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) can be converted (dehydrated) to anhydrous  $\text{CaHPO}_4$  by heating ( $65$ – $104^\circ\text{C}$ ) in aqueous medium, preferably in its own mother liquor. This is unexpected because crystals would usually become hydrous under such conditions. The anhydrous calcium hydrogen phosphate has a high degree of crystallinity, relatively uniformly-sized particles, narrow particle size distribution range, relatively little agglomeration or aggregation, is essentially pure anhydrous calcium hydrogen phosphate and consists of plate-like crystals.

Diammonium phosphate is added to a solution of calcium salt at temperatures below  $65^\circ\text{C}$ , to form crystalline calcium hydrogen phosphate dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ). While still at the temperature of precipitation, the pH of the dihydrate slurry is adjusted with mineral acid. The slurry is then heated to boiling to effect conversion (dehydration) of the  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$  to anhydrous  $\text{CaHPO}_4$ . Conversion is invariably accompanied by a characteristic drop in pH from the value at which the slurry was initially adjusted to a value in the 2.2–3.6 range, depending on the starting pH.

The dihydrate and the resulting anhydrous product are readily identifiable from X-ray data. The conversion (dehydration) can also be readily followed by microscopic examination of the products at each stage.

Product yields range from 50 to 90% of theoretical yield, based on calcium, depending mainly on the pH to which the dihydrate is adjusted (conversion pH) before boiling.

One advantage of the invention is the improvement in the properties of the dibasic calcium phosphate produced, as explained in the foregoing.

A further advantage is the simplicity, ease and convenience of achieving conversion (dehydration) of dihydrate without separation from mother liquor, eliminating costly and time consuming steps which would normally be involved.

Still another advantage is the enhanced performance of fluorescent lamps, manufactured with the product of the invention.

There are numerous modifications and variations in methods which can be used without departing from the spirit of the invention. These, however, are mainly in the category of varying conditions for preparing dihydrate. The basic procedure, i.e., converting dihydrate  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$  to anhydrous  $\text{CaHPO}_4$  by heating ( $65$ – $104^\circ\text{C}$ ) in aqueous medium, preferably mother liquor, is applicable to all such variations.

The sole, critical condition for achieving such conversion (dehydration) of dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) consistently to produce the advantages of the invention is to heat a pH-adjusted dihydrate slurry.

The mixing of boiling solutions of calcium salt and diammonium phosphate (DAP) or mono-ammonium phosphate (MAP), or adding a boiling DAP (or MAP) aqueous solution to a boiling calcium salt solution has been described in a U.S. patent disclosure, Serial No. 827,173, filed July 15, 1959, by Mooney et al. Such methods do not achieve the results of the present invention, for the calcium phosphate precipitated at temperatures greater than  $65^\circ\text{C}$ , has been identified as anhydrous calcium hydrogen orthophosphate. The present invention depends on formation of dihydrate and subsequent dehydration.

Variations such as raw materials, temperature of dihydrate precipitation, conversion pH, mineral acid used to adjust pH and heating period may have an effect on crystal habit, crystal size, size distribution, degree of crystallinity, aggregation and/or agglomeration, yield,

case of recovery by filtration, etc., of the final product but do not in any way affect the implementation of the invention to the dihydrate slurry.

Dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) for use as a starting material in our process may be prepared from a calcium salt solution and diammonium phosphate (DAP) as the source of phosphate ion. The source of phosphate ion may also be mono-ammonium phosphate (MAP) or a mixture of a suitable grade phosphoric acid and ammonium hydroxide. DAP and MAP may be added to calcium salt solution as solids or in solution.

The source of calcium may be any of the common salts which are commercially available, depending on economic considerations. Calcium chloride, calcium nitrate, calcium formate, calcium acetate, calcium carbonate (in phosphoric acid) and even limestone (in phosphoric acid) are all satisfactory sources of calcium.

Dibasic calcium phosphate dihydrate, ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) may be precipitated within the practical range of about 20° C. to 65° C.

Within this range, the temperature is not critical. A preferred and convenient temperature for dihydrate preparation is room temperature, 20-30° C.

Prior to conversion (dehydration) by heating, the pH of the dihydrate slurry may be adjusted to any value ranging from 2.5 to 5.5. For practical reasons, i.e., yield, we have established a lower limit of 3.0 but all of the advantages of the invention may be realized when operating within this range. The pH to which dihydrate slurry is adjusted before conversion affects crystal habit, crystal size and yield. Operating at the lower end of the range tends to give diamond-shaped crystals, larger size crystals but lower yield. Operating at the upper end of the range tends to give cubic crystals of smaller size, and increased yield.

The pH of dihydrate slurry may be adjusted before conversion (dehydration) with either hydrochloric acid, nitric acid, phosphoric acid, or mixtures of any two or three of these acids. We prefer to use nitric acid in systems where calcium nitrate is the starting material, hydrochloric acid where calcium chloride is the starting material.

The concentration of calcium in solution may range from 0.1 molar to 3 molar; similarly, the concentration of DAP may be varied over the same range. We prefer to work at concentrations in the range of 0.5 molar.

The dihydrate slurry may be formed from solutions containing a 1:1 mole ratio of calcium to phosphate (stoichiometric). The starting calcium to phosphate ratio in solution may range from 3:1 down to 1:3.

After suitably adjusting pH and achieving boiling conditions, boiling may range from a few minutes to four hours. The length of the boiling period depends mainly on concentration and the size of the starting dihydrate crystals.

Embodiments of the invention are illustrated in the following specific examples:

#### Example 1

43.2 pounds of calcium was dissolved in 140 gallons of deionized water and total volume was adjusted to 160 gallons. 34.8 pounds of DAP solids (commercial diammonium phosphate) was added to the calcium nitrate solution to form calcium hydrogen phosphate dihydrate at room temperatures (25° C.). A volume of 4650 ml. of concentrated hydrochloric acid was added to adjust the pH of the slurry to 3.6. The slurry was heated to boiling; temperature was recorded at 101-103° C. After 5 minutes there occurred a characteristic drop in pH to 2.5-2.6, indicating conversion (dehydration). Conversion was confirmed by microscopic examination. A yield of 16 pounds of dry product was obtained, equivalent to 64.5% of theoretical (24.9 pounds) based on calcium. The product consisted of diamond-shaped, plate-like crystals which were relatively non-agglomerated.

#### Example 2

314.8 pounds of calcium nitrate was dissolved in 140 gallons of deionized water and total volume was adjusted to 160 gallons. 175.7 pounds of DAP solids was added to the calcium nitrate solution to form dihydrate at room temperature. The dihydrate slurry was adjusted to a pH of 2.9 with 10,000 ml. of reagent  $\text{HNO}_3$ . The slurry was heated to boiling and after one-half hour there occurred a characteristic pH drop to about 2.1, indicating conversion or dehydration. This was confirmed by microscopic examination of the product. A yield of 128 pounds, 70.3% of theoretical (183 pounds) based on calcium was obtained. The product consisted of diamond-shaped, plate-like crystals.

#### Example 3

48 pounds of purified calcium chloride was dissolved in 140 gallons of deionized water and total volume was adjusted to 160 gallons. 57.3 pounds of DAP solids were added to the calcium chloride solution to form dihydrate at room temperature. The dihydrate slurry was adjusted to a pH of 3.6 with 3,000 ml. of reagent hydrochloric acid. The slurry was heated to boiling and maintained at boiling until there occurred the characteristic pH drop to 2.9, indicating conversion. Total time at boiling was about one hour. Conversion was confirmed by microscopic examination. The product consisted of highly-crystalline, diamond-shaped, plate-like crystals. Yield was 44 pounds equivalent to 74.5% of theoretical (59 pounds) based on calcium.

#### Example 4

148 pounds of purified  $\text{CaCl}_2$  was dissolved in 140 gallons of deionized water and total volume was adjusted to 160 gallons. 175.7 pounds of DAP solids were added to the chloride solution at room temperature (25° C.) to form dihydrate. The dihydrate slurry was adjusted at room temperature to a pH of 3.8 with 4,000 ml. of hydrochloric acid. The slurry was heated to a boiling and maintained at boiling until there occurred a characteristic drop in pH of 2.5-2.6, indicating conversion. Total time at boiling was about one hour. Conversion was confirmed by microscopic examination of the product. The product consisted of highly-crystalline, diamond-shaped, plate-like crystals and crystal size tended to be small. Yield was 159 pounds, 87.7% of theoretical (181 pounds) based on calcium.

#### Example 5

50 62.8 pounds of calcium nitrate was dissolved in 140 gallons of deionized water and total volume was adjusted to 160 gallons. 69.6 pounds of DAP solids was added to the nitrate solution at room temperature to form dihydrate. The dihydrate slurry was adjusted to a pH of 4.4 with 1100 ml. of nitric acid. The slurry was heated to boiling until there occurred a characteristic drop in pH to 3.5. Total time at boiling was about one hour. Conversion was confirmed by microscopic examination. The product was highly crystalline; crystals were plate-like but had a cubic and sod-like crystal habit. This illustrates change in habit with high conversion pH values. Yield was 32 pounds or 88.6% of theoretical, illustrating a trend to higher yield with higher conversion pH values.

The range of temperatures given for heating in the foregoing examples do not exceed 104° C. However, if the ambient pressure, which will generally be atmospheric, is high, the boiling point of the heated material may be somewhat above 104° C., and the mixture can be heated to the higher boiling point. However, higher pressures than standard atmospheric will not ordinarily be desirable.

What we claim is:

1. A process of converting calcium hydrogen phosphate dihydrate to anhydrous calcium hydrogen phos-

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phate, which process comprises adjusting the pH of the dihydrate in its own mother liquor to a value between about 2.5 to 5.5, by adding acid, then heating the dihydrate in its own mother liquor to a temperature between about 65° C. and its boiling point until the pH drops substantially below its initial value to a value between about 2.2 to 3.6, and recovering the resultant anhydrous phosphate from the remaining mother liquor.

2. A process of converting calcium hydrogen phosphate dihydrate to anhydrous calcium hydrogen phosphate, which process comprises adjusting the pH of the dihydrate in an aqueous medium to a value between about

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2.5 to 5.5 by adding acid, then heating the dihydrate in the aqueous medium to a temperature between about 65° C. and its boiling point until the pH drops substantially below its initial value to a value between about 2.2 to 3.6, and recovering the resultant anhydrous phosphate from the aqueous medium.

References Cited in the file of this patent

- 10 Van Wazer: Phosphorus and its Compounds, vol. 1, Chemistry, Interscience Publishers, N.Y., 1958, pages 519-522.

**X. RELATED PROCEEDINGS APPENDIX**

None.